

Preliminary Amendment

National Stage Entry of PCT/AU2003/001446

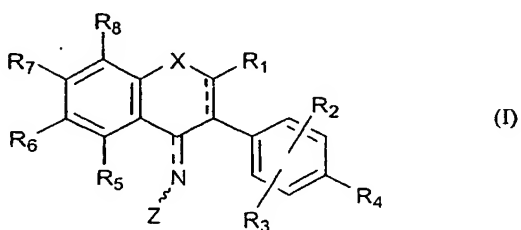
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AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. (original): A compound of the general formula (I):



wherein

- R₁, R₂, R₃, R₄, R₅, R₆, R₇ and R₈ are independently hydrogen, hydroxy, OR₉, OC(O)H, OC(O)R₉, OS(O)R₉, OSi(R₁₀)₃, C(O)R₁₁, CO₂R₁₂, alkyl, haloalkyl, aryl, arylalkyl, thio, alkylthio, amino, alkylamino, dialkylamino, nitro or halo, or any two of the substituents R₂ R₃ and R₄ together with the carbon atoms to which they are attached form a cyclic alkyl, cyclic heteroalkyl, aryl or heteroaryl structure,
- R₉ is alkyl, haloalkyl, aryl, arylalkyl or alkylaryl,
- R₁₀ is independently hydrogen, alkyl or aryl,
- R₁₁ is hydrogen, alkyl, aryl, arylalkyl, arylalkyl or an amino acid, and
- R₁₂ is hydrogen, alkyl, haloalkyl, aryl, arylalkyl or alkylaryl,
- X is O, NR₁₂ or S,
- Z is R₁₃, NR₁₄R₁₅, NR₁₃CONR₁₄R₁₅, N=CR₁₆R₁₇ or OR₁₃,
- R₁₃, R₁₄ and R₁₅ are independently hydrogen, amino, thio, nitro, cyano, or optionally substituted alkyl, haloalkyl, acyl, aryl, heteroaryl, arylalkyl or alkylaryl, or the substituents R₁₄ and R₁₅ together with the nitrogen atom to which they are attached form an optionally substituted cyclic heteroalkyl or heteroaromatic structure, and
- R₁₆ and R₁₇ are independently hydrogen, amino, thio, nitro, cyano, or optionally substituted alkyl, haloalkyl, acyl, aryl, heteroaryl, arylalkyl or alkylaryl, or the substituents R₁₆

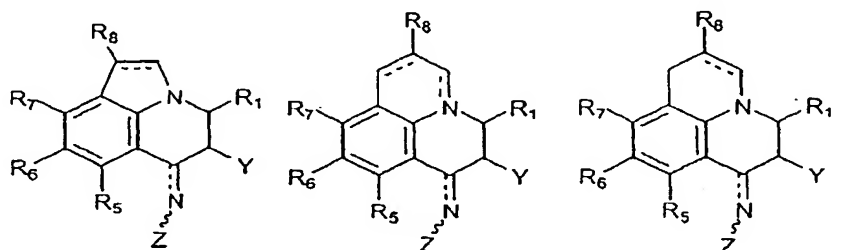
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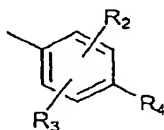
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and R_{17} taken together with the carbon atom to which they are attached form an optionally substituted isoflavonoid ring system,

or when X is NR_{12} , the substituent R_{12} maybe a bond such that R_8 and X together with the carbon atoms to which they are attached form one of the following structures:



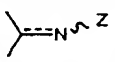
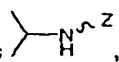
where Y is



and wherein

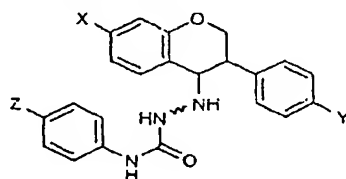
R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 and Z are as defined above, and

the drawing "=" represents either a single bond or a double bond and when it is a single

bond, the drawing  represents .

which compounds include pharmaceutically acceptable salts and derivatives thereof

with the proviso that compounds of the formula



wherein

X is F or Cl,

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Y is H or F, and

Z is Cl, Br or CF₃

are specifically excluded, and

with the proviso that the following compounds

3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-amine

N-(3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-yl)- α -phenyl-benzeneacetamide N-[3,4-Dihydro-3-(4-hydroxyphenyl)-2H-1-benzopyran-4-yl]- α -phenyl-benzeneacetamide 2,3-Dihydro-3-phenyl-4H-1-benzopyran-4-one oxime

2,3-Dihydro-3-phenyl-4H-1-benzopyran-4-one O-acetyloxime N-[3-(3,4-

Ditnethoxyphenyl)-3,4-dihydro-7,8-dimethoxy-2H-1-benzopyran-4-yl]formamide

2,3-Dihydro-2,3-diphenyl-4H-1-benzopyran-4-one hydrazone 4',7-

Dimethoxy-isoflavanone oxime 3,4-Dihydro-3-phenyl-2H-1-

benzopyran-4-amine N-(3-Phenyl-4-chromanyl)-acetamide N-(7-

Methoxy-3-phenyl-4-chromanyl)-acetamide 4',7-Dimethoxy-4-

isoflavanamine N-[7-Methoxy-3-(p-methoxyphenyl)-4-chromanyl]-

acetamide 7-Methoxy-3-isoflavanamine

2'-Hydroxy-isoflavanone (2,4-dinitrophenyl)hydrazone 7-

Methoxy-isoflavanone oxime

7-Methoxy-3',4'-(methylenedioxy)-isoflavanone (2,4-dinitrophenyl)hydrazone 7-

Methoxy-isoflavanone phenylhydrazone 5,7-Dimethoxy-isoflavanone (2,4-

dinitrophenyl)hydrazone 2,3-Dihydro-3-phenyl-4H-1-benzopyran-4-one oxime

Isoflavanone (2,4-dinitrophenyl) hydrazone 6-Hydroxy-

isoflavanone

(2,4-dinitrophenyl) hydrazone

7-Hydroxy-isoflavanone (2,4-dinitrophenyl) hydrazone

Isoflavanone semicarbazone

7-Methoxy-3',4'-(methylenedioxy)-isoflavanone (2,4-dinitrophenyl)hydrazone

7-Hydroxy-3',4'-(methylenedioxy)-isoflavanone (2,4-dinitrophenyl)hydrazone

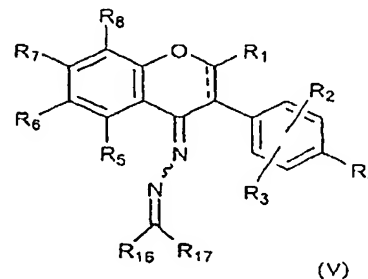
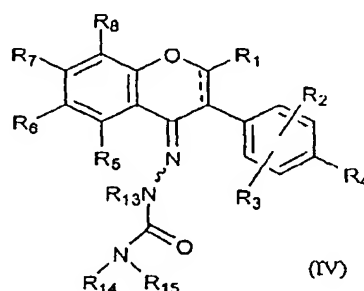
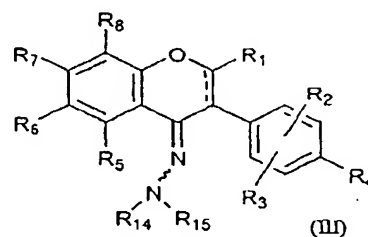
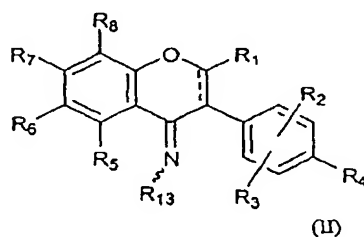
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7-Methoxy-isoflavanone (2,4-dinitrophenyl)hydrazone 7-Hydroxy-4'-methoxy-isoflavanone (2,4-dinitrophenyl)hydrazone 5,7-Dimethoxy-isoflavanone (2,4-dinitrophenyl)hydrazone
6-Methoxy-isoflavanone (2,4-dinitrophenyl)hydrazone 4',5,7-trimethoxy-isoflavanone (2,4-dinitrophenyl)hydrazone 7-Methoxy-2-methyl-isoflavanone (2,4-dinitrophenyl)hydrazone 2-(Hydroxymethyl)-7-methoxy-isoflavanone (2,4-dinitrophenyl)hydrazone and hydrochloride salts thereof are specifically excluded.

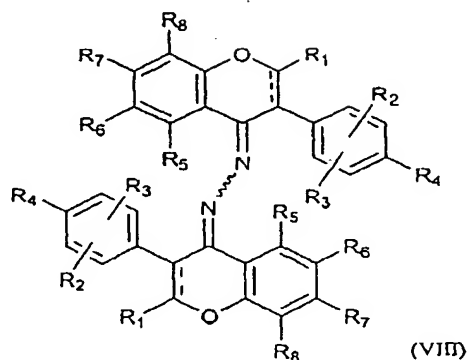
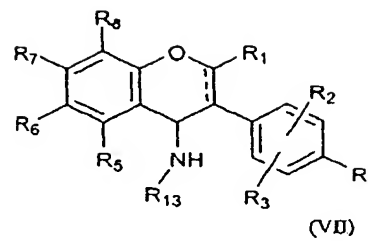
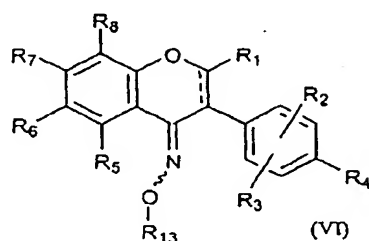
2. (original): A compound according to claim 1, depicted by one of the general formulae (II)-(VIII):



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wherein

R₁, R₂, R₃, R₄, R₅, R₆, R₇ and R₈ are independently hydrogen, hydroxy, OR₉, OC(O)R₉, OS(O)R₉, alkyl, aryl, arylalkyl, thio, alkylthio, bromo, chloro or fluoro, R₉ is alkyl, fluoroalkyl or arylalkyl,

R₁₃, R₁₄ and R₁₅ are independently hydrogen, amino, cyano, thio, nitro, or optionally substituted alkyl, haloalkyl, acyl, aryl, arylalkyl or alkylaryl, or the substituents R₁₄ and R₁₅ together with the nitrogen atom to which they are attached form an optionally substituted cyclic heteroalkyl or heteroaromatic structure,

R₁₆ and R₁₇ are independently hydrogen, amino, cyano, thio, nitro or optionally substituted alkyl, haloalkyl, aryl, aryl, arylalkyl or alkylaryl, or the substituents R₁₆ and R₁₇, taken together with the carbon atom to which they are attached form an optionally substituted isoflavonoid ring system, and

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the drawing "—" represents either a single bond or a double bond.

3. (original): A compound according to claim 2, wherein

R₁ is hydrogen,

R₂, R₃, R₅, R₆ and R₈ are independently hydrogen, hydroxy, OR₉, OC(O)R₉, alkyl, aryl or arylalkyl

R₄ and R₇ are independently hydroxy, OR₉ or OC(O)R₉,

R₉ is methyl, ethyl, propyl, isopropyl or trifluoromethyl, and

R₁₃, R₁₄ and R₁₅ are independently hydrogen, methyl, ethyl, propyl, isopropyl, trifluoromethyl or optionally substituted phenyl, naphthyl or benzyl, or the substituents R₁₄ and R₁₅ together with the nitrogen atom to which they are attached form an optionally substituted cyclic heteroalkyl or heteroaromatic structure,

R₁₆ and R₁₇ are independently hydrogen, methyl, ethyl, propyl, isopropyl, trifluoromethyl or optionally substituted phenyl, naphthyl or benzyl, or the substituents R₁₆ and R₁₇ taken together with the carbon atom to which they are attached form an optionally substituted isoflavonoid ring system, and

the drawing "—" represents either a single bond or a double bond.

4. (original): A compound according to claim 3,

wherein R₁ is hydrogen,

R₂, R₃, R₅, R₆ and R₈ are independently hydrogen, hydroxy, OR₉, OC(O)R₉ or methyl, R₄ and R₇ are independently hydroxy, OR₉ or OC(O)R₉, R₉ is methyl,

R₁₃ is hydrogen, methyl, ethyl, trifluoromethyl, phenyl, chlorophenyl, nitrophenyl, toluyl, naphthyl, benzyl, chlorobenzyl, nitrobenzyl or methylbenzyl,

R₁₄ is hydrogen and R₁₅ is hydrogen, methyl, ethyl, trifluoromethyl, phenyl, chlorophenyl, nitrophenyl, toluyl, naphthyl, benzyl, chlorobenzyl, nitrobenzyl or

methylbenzyl, or the substituents R₁₄ and R₁₅ together with the nitrogen atom to which they are attached form an optionally substituted cyclic heteroalkyl or heteroaromatic structure, R₁₆ and R₁₇ are independently hydrogen, methyl, ethyl, trifluoromethyl, phenyl, chlorophenyl, nitrophenyl, toluyl, naphthyl, benzyl, chlorobenzyl, nitrobenzyl or methylbenzyl, or the substituents R₁₆ and R₁₇ taken together with the carbon atom to which they are attached form an optionally substituted isoflavonoid ring system, and the drawing "—" represents a single bond.

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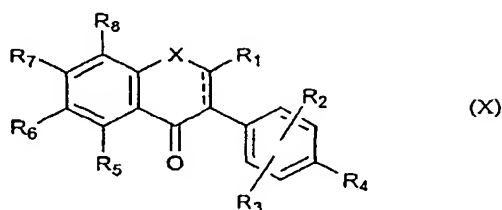
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5. (original): A compound according to claim 4 selected from compounds (1) - (14):

4',7-Dihydroxyisoflavanone (phenyl)hydrazone (1)
4',7-Dihydroxyisoflavanone (4-nitrophenyl)hydrazone (2)
4',7-Dihydroxyisoflavanone (4-methylphenyl)hydrazone (3)
4',7-Dihydroxyisoflavanone (benzyl)hydrazone (4)
4',7-Dihydroxyisoflavanone (4',7-dihydroxyisoflavanone)hydrazone (5)
4',7-Dihydroxyisoflavanone (2-chlorophenyl)hydrazone (6)
4',7-Dihydroxyisoflavanone (3-chlorophenyl)hydrazone (7)
4',7-Dihydroxyisoflavanone (4-chlorophenyl)hydrazone (8)
4',7-Dihydroxyisoflavanone (2-pyridyl)hydrazone (9)
4',7-Dihydroxyisoflavanone (4-cyanophenyl)hydrazone (10)
4',7-Dihydroxy-4-methylimino-isoflavan (11)
4',7-Dihydroxyisoflavanone oxime (12)
4-Amino-3',4'-dimethoxy-7-hydroxy-8-methylisoflavan (13)
N-[3',4'-dimethoxy-7-hydroxy-8-methyl-4-chromanyl]-acetamide (14)
which compounds include pharmaceutically acceptable salts thereof.

6. (currently amended): A process for the preparation of a compound of formula (I) as claimed in ~~any one of claims 1 to 5~~ claim 1 comprising the step of reacting the 4-keto group of a compound of the formula (X):



wherein

R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈ and X are as defined in claim 1, and

the drawing “---” represents either a single bond or a double bond, with an aminating agent.

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7. (original): A method for the treatment, prophylaxis or amelioration of a disease or disorder which method includes the step of administering a therapeutically effective amount of one or more compounds of formula (1) or a pharmaceutically acceptable salt or derivative thereof to a subject,

with the proviso that the compounds and pharmaceutically acceptable salts of 3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-amine

N-(3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-yl)- α -phenyl-benzeneacetamide, and N-[3,4-Dihydro-3-(4-hydroxyphenyl)-2H-1-benzopyran-4-yl]- α -phenyl-benzeneacetamide are disclaimed for the treatment, prophylaxis or amelioration of atherosclerosis.

8. (original): A method for the treatment, prevention or amelioration of diseases associated with aberrant cell survival, aberrant cell proliferation, abnormal cellular migration, abnormal angiogenesis, abnormal estrogen/androgen balance, dysfunctional or abnormal steroid genesis, degeneration including degenerative changes within blood vessel walls, inflammation, and immunological imbalance, which comprises administering to a subject one or more compounds of the formula (I) or a pharmaceutically acceptable salt or derivative thereof optionally in association with a carrier and/or excipient, with the proviso that the compounds and pharmaceutically acceptable salts of 3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-amine N-(3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-yl)- α -phenyl-benzeneacetamide, and N-[3,4-Dihydro-3-(4-hydroxyphenyl)-2H-1-benzopyran-4-yl]- α -phenyl-benzeneacetamide are disclaimed for the treatment, prophylaxis or amelioration of atherosclerosis.

9. (original): A method of inducing apoptosis in cells expressing abnormal pro-survival phenotype which comprises contacting said cells with one or more compounds of the formula (I) or a pharmaceutically acceptable salt or derivative thereof optionally in association with a carrier or excipient.

10. (original): A method for inhibiting migration of cells having an abnormal cellular migration phenotype which comprises contacting said cells with a compound of the formula (1) or a pharmaceutically acceptable salt or derivative thereof optionally in association with a carrier or excipient.

11. (original): A method for inhibiting angiogenesis in tissue expressing aberrant angiogenic phenotype which comprises contacting said tissue with a compound of the formula

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(I) or a pharmaceutically acceptable salt or derivative thereof optionally in association with a carrier or excipient,

with the proviso that the compounds and pharmaceutically acceptable salts of

3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-amine

N-(3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-yl)- α -phenyl-benzeneacetamide, and

N-[3,4-Dihydro-3-(4-hydroxyphenyl)-2H-1-benzopyran-4-yl]- α -phenyl-benzeneacetamide are disclaimed for the treatment, prophylaxis or amelioration of atherosclerosis.

12. (original): A method for the treatment, prevention or amelioration of cancer in a mammal which method comprises the step of bringing a compound of formula (I) or a pharmaceutically acceptable salt or derivative thereof into contact with cancerous tissue in a mammal that is suffering from a tumour, such that neoplastic development in said cancerous tissue is retarded or arrested.

13. (canceled).

14. (canceled).

15. (original): An agent for the treatment, prophylaxis or amelioration of a disease or disorder, which agent comprises one or more compounds of formula (I) or a pharmaceutically acceptable salt or derivative thereof,

with the proviso that the compounds and pharmaceutically acceptable salts of 3,4-

Dihydro-3-phenyl-2H-1-benzopyran-4-amine

N-(3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-yl)- α -phenyl-benzeneacetamide, and

N-[3,4-Dihydro-3-(4-hydroxyphenyl)-2H-1-benzopyran-4-yl]- α -phenyl-benzeneacetamide are disclaimed for the treatment, prophylaxis or amelioration of atherosclerosis.

16. (original): A pharmaceutical composition which comprises one or more compounds of formula (I) or a pharmaceutically acceptable salt or derivative thereof in association with one or more pharmaceutical carriers, excipients, auxiliaries and/or diluents, with the proviso that the compounds and pharmaceutically acceptable salts of 3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-amine N-(3,4-Dihydro-3-phenyl-2H-1-benzopyran-4-yl)- α -phenyl-benzeneacetamide, and N-[3,4-Dihydro-3-(4-hydroxyphenyl)-2H-1-benzopyran-4-yl]- α -phenyl-benzeneacetamide are

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disclaimed.

17. (original): A drink or food-stuff, which contains one or more compounds of formula (1) or a pharmaceutically acceptable salt or derivative thereof.

18. (original): A compound of formula (I) or a pharmaceutically acceptable salt thereof as herein described with reference to the Examples and/or accompanying drawings.